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Isotope Effects on the Ring Inversion of Cyclooctatetraene

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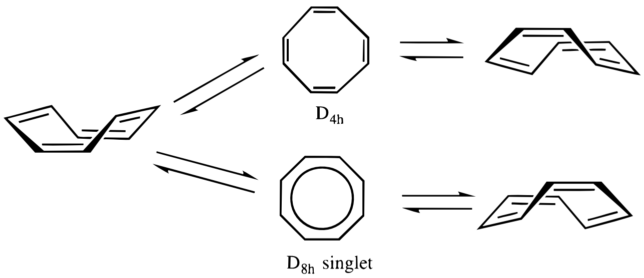
Abstract: ^{1}H NMR studies (400 MHz) on isopropoxycyclooctatetraene (C_8H_7-O-C_3H_7) and its ring-d_7 analogue (C_8D_7-O-C_3H_7) show that there is an inverse isotope effect on the rate of ring inversion of $k_H/k_D = 0.68-0.57$ in the temperature range from −10 to −50 °C. These experiments confirm the validity of previously published DFT calculations on cyclooctatetraene/cyclooctatetraene-d_8, which predict an inverse isotope effect of about this size on the rate of ring inversion in this temperature range. The large inverse isotope effect upon ring inversion explains why the similarly large normal equilibrium isotope effect, found in the reduction of benzene to its corresponding anion radical, is not observed in the analogous reduction of cyclooctatetraene.

Due to the fact that cyclooctatetraene (COT) is the smallest, stable, nonaromatic annulene, COT and its derivatives have been intensively studied.[1] Of particular interest have been the dynamical processes by which tub-shaped (D_{2d}) COT undergoes ring inversion and bond shift.[2,3]

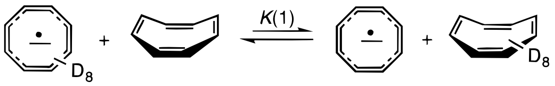
From the time of Anet's first NMR studies of ring inversion,[2] it has been assumed that this process proceeds through a D_{4h} transition state in which the COT ring is planar and has alternating long and short C−C bonds, as shown in Scheme 1. Whether bond shifting[4] proceeds via a D_{8h} transition state, in which the COT ring is not only planar but also has equal C−C bond lengths, has been more controversial.[5] However, negative ion photoelectron (PE) spectroscopy gives every indication that bond shifting in COT does, indeed, occur via such a transition state.[6] MCSCF(8,8)/6-31G* calculations on COT predict D_{4h} and D_{8h} transition states for respectively ring inversion and bond shifting.[7,8]

Scheme 1



Calculations[9] and experiments[6,10] also both agree that, unlike neutral COT, the radical anion of COT (COT$^{\bullet-}$) is planar. COT$^{\bullet-}$ is predicted to undergo rapid interconversion between a pair of D_{4h} equilibrium geometries, with unequal bond lengths, via D_{4h} transition state geometries, with equal bond lengths but unequal bond angles.[9]

The planarization of COT that occurs upon addition of an electron to form COT$^{\bullet-}$ has been calculated to have a profound effect on the equilibrium isotope effect for the transfer of an electron from the perdeuterio anion radical to the perprotio neutral molecule (reaction 1).[11] At 173 K, the equilibrium constant for this reaction is $K(1) = 0.86$, which corresponds to $\Delta G°(1) = 0.05$ kcal/mol at this temperature.[12]



(1)

The free energy change for reaction 1 is much smaller in magnitude than the free energy changes for the analogous equilibria involving benzene (reaction 2) and a wide variety of

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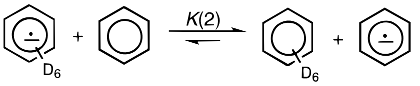
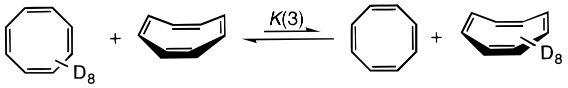
other aromatic systems.[13] At 173 K the equilibrium constant for reaction 2 is $K(2) = 3.85$,[13e] which corresponds to a standard free energy change of $\Delta G°(2) = -0.47$ kcal/mol at this temperature.



(2)

Our DFT calculations[11] not only reproduced the experimental trends in both the benzene and COT systems,[14] but they also offered an explanation of the large difference between the equilibrium isotope effects found for reactions 1 and 2. The calculations find that, like reaction 2, reaction 1 does have a large normal isotope effect, *but only when COT is constrained to planarity*. The small isotope effect, both found[12] and calculated[11] for this reaction when COT and COT-d_8 are at their tub-shaped equilibrium geometries, is attributable to an inverse isotope effect on the planarization of COT (reaction 3), which is of similar size to the large normal isotope effect on the reduction of *planar* COT.



(3)

Using B3LYP/6-31+G* frequencies in the Bigeleisen equation,[15] the calculations predict an isotope effect on the planarization of COT of $K(3) = 0.41$ at 173 K.[11] This means that the frequencies of the vibrations that involve significant motions of the hydrogens must, in general, be higher at the D_{4h} planar geometry of COT than at the tub-shaped (D_{2d}) equilibrium geometry. The origin of the higher C−H bending frequencies computed for planar than for tub-shaped COT is, presumably, the change in hybridization at the eight carbons that occurs on planarization. The increase in the size of the internal C−C−C bond angles upon planarization suggests that the amount of carbon 2s character in the C−C bonds increases. This results in an increase in the amount of 2p character in the C−H bonds, which increases the C−H bending frequencies.

Values of $K(3)$ calculated at five temperatures between 123 and 298 K fit eq 4 with $R^2 = 1.000$. Since a planar geometry is the transition state for ring inversion of COT, $K(3)$ is equal

$$\ln K(3) = 0.21 - (0.38\ \text{kcal/mol})/RT \qquad (4)$$

to the ratio of the rate constants, k_H/k_D, for this process. Therefore, the theoretical explanation of the large experimental difference between $K(1)$ and $K(2)$ in eqs 1 and 2 can, at least in principle, be tested experimentally by measuring the kinetic isotope effect on the rates of ring inversion of COT and COT-d_8.

In practice, a derivative of COT with diastereotopic nuclei is required to measure the rate of ring inversion.[2,3] Therefore, we have prepared isopropyl ethers from COT and COT-d_8 and compared the rates at which the diastereotopic methyl protons in isopropoxy-COT and isopropoxy-COT-d_7 undergo site exchange by inversion of the eight-membered ring (reaction 5 with R = H and R = D, respectively). Herein we report the results of these studies.

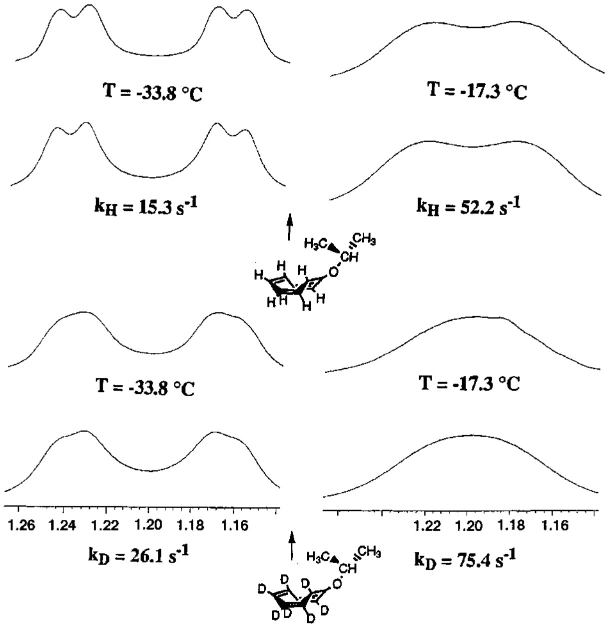
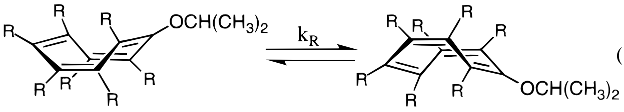


Figure 1. NMR spectra (400 MHz) of the methyl groups of C_8D_7-O-C_3H_7 (lower) and C_8H_7-O-C_3H_7 (upper) at −17.3 and −33.8 °C. The computer-generated simulations are shown directly below each experimental spectrum. The rate constants for the interconversion of the methyl groups (k_D or k_H) are shown directly below the simulations. The errors in the rate constants, given in Table 1, were obtained by generating simulations at each temperature, using rate constants that were clearly too large and too small.



(5)

Results

At ambient temperatures methyl group site exchange is fast on the NMR time scale at 400 MHz. The ^{1}H NMR spectra of both isopropoxy-COT and isopropoxy-COT-d_7 show a single resonance for the diastereotopic methyl protons, split into a doublet with $J = 6.0$ Hz by the methine proton.

At −33.8 °C, as shown in Figure 1, the pair of doublets for the two nonequivalent methyl groups ($\delta = 1.23$ and 1.16 ppm) is resolved in the spectrum of the undeuterated ether; but only two broad peaks are observed in the spectrum of the heptadeuterio compound. Figure 1 also shows that at −17.3 °C the ^{1}H NMR spectrum of isopropoxy-COT-d_7 is coalesced into a single broad line, while the undeuterated ether still exhibits two broad but distinct peaks for the diastereotopic methyl protons.

The spectra in Figure 1 clearly reveal that, as predicted by our calculations,[11] deuteriation of the COT ring accelerates the ring inversion process. Computer simulation of the spectrum at −33.8 °C (Figure 1) shows that methyl group interconversion is 1.7 times faster when the ring protons in isopropoxy-COT are replaced by deuteriums. Equation 3, which gives the calculated isotope effect on the ring inversion of COT/COT-d_8, predicts faster ring inversion in COT-d_8 than in COT by a factor of 1.8 at this temperature. Hence, the NMR data and

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Table 1. Rate Constants for Ring Inversion (in s^{-1}) at Various Temperatures (°C) for the Perprotiated (k_H) and Ring Deuterated (k_D) Isopropoxycyclooctatetraenes and the k_H Rate Constants Obtained by Oth[a]

temp	k_H	k_D	$k_{H(Oth)}$
−50.4	4.2 ± 0.5	6.5 ± 0.3	1.9
−44.9	6.0 ± 0.3		3.7
−39.3	9.0 ± 0.4		7.2
−33.8	15.3 ± 0.5	26.1 ± 0.3	13.5
−28.3	20.5 ± 1.5	33.5 ± 0.9	24.4
−22.8	35.0 ± 1.0	50.0 ± 0.8	43.1
−20.1	41.0 ± 3.0	62.4 ± 1.2	56.5
−17.3	52.2 ± 0.8	75.4 ± 1.4	74.3
−11.8	80.9 ± 2.1	118.0 ± 3	125.2

[a] Oth reported $k_H = 361\ s^{-1}$ at 0 °C and an E_a of 12.61 kcal/mol.[12] His k_H values at the other temperatures were calculated from these parameters.

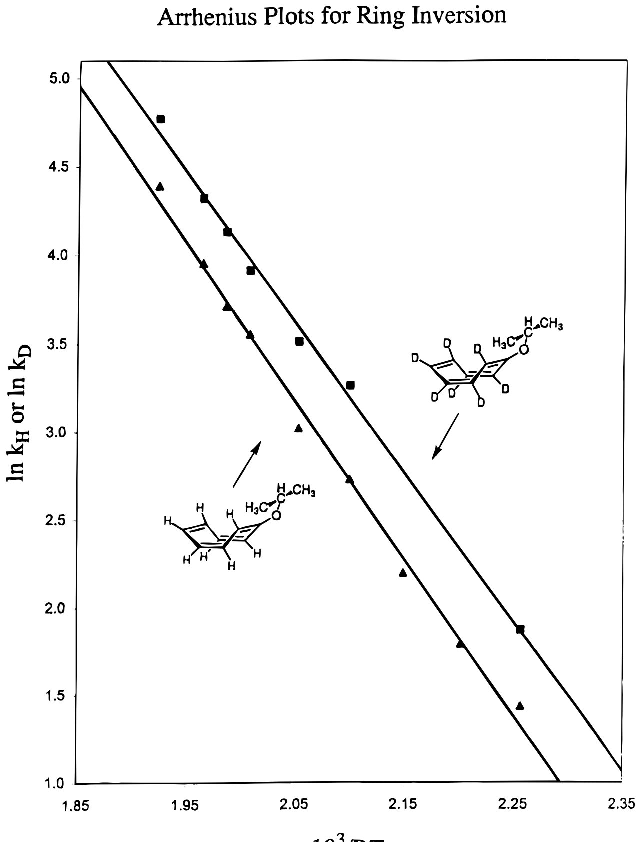

Figure 2. Plots of ln k_D and ln k_H for ring inversion vs $10^3/RT$. The equations for the lines that provide the best least-squares fits ($R^2 = 0.996$) to the experimental data are ln $k_H = 23.72 - (10.14\ \text{kcal/mol})/RT$ and ln $k_D = 23.15 - (9.65\ \text{kcal/mol})/RT$.

the quantum mechanical predictions are in very good agreement at this temperature.

To obtain more quantitative data on the inverse isotope effect on the rate of ring inversion of isopropoxy-COT-d_7, we obtained ^1H NMR spectra of the deuterated and undeuterated compounds at seven temperatures from −11.8 to −50.4 °C. The rate constants for methyl site exchange were obtained by simulations and are given in Table 1. Arrhenius plots of the rate constants, which are shown in Figure 2 for the deuterated and undeuterated compounds, are linear with $R^2 = 0.996$ for both lines.

The expression for the temperature dependence of the isotope effect on the ring inversion of isopropoxy-COT-d_7 can be obtained from the equations for the two lines in Figure 2. The resulting values of k_H/k_D at several temperatures are compared in Table 2 with the values predicted for $K(3)$ from eq 4. Also given are the predicted values for the kinetic isotope effect on the ring inversion of COT/COT-d_7. Not surprisingly, the latter values [$K(3)$-d_7] are in better agreement than the former with the experimental values of k_H/k_D for ring inversion of isopropoxy-COT/isopropoxy-COT-d_7.

Table 2. Values of $K(3)$ for COT/COT-d_8[a] and $K(3)$-d_7 for COT/COT-d_7[b] at Several Temperatures and Values of k_H/k_D from the Plots of the Rate Constants for Ring Inversion of Isopropoxy-COT/Isopropoxy-COT-d_7 in Figure 2

T (°C)	$K(3)$	$K(3)$-d_7	k_H/k_D
−10	0.60	0.63	0.69
−20	0.58	0.61	0.67
−30	0.56	0.59	0.64
−40	0.54	0.57	0.61
−50	0.52	0.55	0.59
−100	0.41	0.44	0.43

[a] From eq 4. Computed from ln $K(3)$-$d_7 = 0.22 - (0.36\ \text{kcal/mol})/RT$, which fits the calculated values of $K(3)$ for ring inversion of COT/COT-d_7 at several temperatures with $R^2 = 1.000$.

The excellent agreement between the calculated value of [$K(3)$-d_7] and the extrapolated value of k_H/k_D for ring inversion of isopropoxy-COT/isopropoxy-COT-d_7 at −100 °C suggests that at this temperature k_H/k_D for ring inversion of COT/COT-d_8 is probably quite close to the calculated value of $K(3) = 0.41$. Combining this value with the experimental value of $K(1) = 0.86$ for the reduction of COT/COT-d_8, the reduction of *planar* COT/COT-d_8 is expected to have a normal isotope effect of $K(1)_{planar} = 2.1$. This is a substantial isotope effect; but, as predicted by our previous calculations,[11] it is not as large as the value of $K(2) = 3.85$ that was measured at this temperature for reduction of benzene/benzene-d_6.[13e]

As shown in Table 1, our rate constants for ring inversion in undeuterated isopropoxy-COT are significantly different from those reported by Oth.[3] We believe that the discrepancy comes from the frequency difference between the 60 MHz spectrometer that he used and the 400 MHz spectrometer that we were able to employ for making the same measurements some 27 years later.

We have used the chemical shifts, coupling constants, and exchange rates that we obtained from our 400 MHz spectra to simulate the spectra that Oth would have observed at 60 MHz. Our simulations show that, using a 60 MHz spectrometer, Oth would have been unable to resolve completely the inner two peaks of the two doublets that are due to the diastereotopic methyl groups, even at the lowest temperature (−71 °C) at which he obtained spectra. This would have resulted in some ambiguity concerning the exact difference in the chemical shift of the two methyl groups. This problem would have been compounded by the fact that our simulations of his 60 MHz spectra show the two inner peaks undergo coalescence at a lower temperature than do the outer two peaks.

In contrast, with a 400 MHz spectrometer, the two doublets are well separated at low temperatures; so an accurate chemical shift difference between them is easy to obtain. In addition, as shown in Figure 1, at 400 MHz site exchange causes the doublets due to J coupling to coalesce first, followed by coalescence of the two broad singlets that result from the chemical shift difference. The latter effect of using a much higher field spectrometer than the one available to Oth makes fitting of simulated spectra to those observed much more sensitive to the rates used in the simulations.

Conclusions

The dynamic NMR spectra of isopropoxy-COT and isopropoxy-COT-d_7 show that, as predicted,[11] there is a large inverse isotope effect on the rate of ring inversion. From Table 2, it is clear that the size of this effect is about that expected, based on calculations of the kinetic isotope effect for ring inversion of COT/COT-d_8. The results of our NMR study provide strong support for the computationally based explanation[11] of the difference between the small inverse, equilibrium isotope effect measured for reduction of COT[12] and the large normal, equilibrium isotope effects found for reduction of planar aromatic molecules, such as benzene.[13]

Experimental Section

Perdeuterated COT was prepared via the Reppe synthesis,[16] as customized in our laboratory[12,17] for use with deuterated acetylene (Aldrich Chemical Co.). Mass spectral analysis was consistent with formation of COT-d_8, containing 5% COT-d_7.

The synthesis of isopropoxy-COT-d_8 was based on Kreb's preparation of *tert*-butoxycyclooctatetraene.[18] A 1.2 g sample of COT-d_8 was brominated, to yield perdeuterated dibromocyclooctatriene, which was then dehydrohalogenated with potassium *tert*-butoxide to yield perdeuterated monobromocyclooctatetraene.

Potassium isopropoxide was prepared by dropwise addition of 10 mL of 2-propanol to a stirred solution of an excess of potassium metal in THF. The mixture was subsequently refluxed for 6 h in an argon atmosphere. The resulting alkoxide solution was then added dropwise to a stirred solution of 0.87 g of perdeuterated bromocyclooctatetraene in THF at −79 °C under an argon atmosphere. After the addition was complete, the solution was allowed to warm to room temperature, and the THF was removed under reduced pressure. The resulting isopropoxy-COT-d_7 (0.5 g yield) was purified via vacuum distillation (1 Torr and 45 to 50 °C). Mass spectral analysis (parent peak at 154 *m*/*e*) was consistent with $C_8D_7OC_3H_7$ at 95% isotopic purity. Undeuterated isopropoxy-COT was generated from cyclooctatetraene (Aldrich Chemical Co.) in the same manner.

NMR spectra were recorded on a Varian Mercury 400 MHz spectrometer. The variable-temperature system was calibrated with a methanol standard.[19] The NMR simulations were generated with the gNMR v.4.0 program.[20]

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